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ORIGINAL ARTICLE

Inhalation of Sevoflurane versus Intravenous Ketamine, Midazolam and Propofol For Sedation in Pediatrics Undergoing Upper Gastrointestinal Endoscopy

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ABSTRACT

Background: Many anesthetics and sedative drugs can be used for sedation in upper gastrointestinal endoscopy (UGE) in pediatrics, however recovery profile and safety are priorities. Objectives: To compare the recovery profile from sedation and complications of sevoflurane inhalation with intravenous ketamine, midazolam and propofol combination for sedation in pediatrics scheduled for elective UGE. Patients and methods: This prospective randomized comparative study included 74 pediatric patients aged one to four years old, ASA I or II who were scheduled for an elective UGE. They were randomly allocated into two groups; Group S (n=37): received inhalational 7% sevoflurane in oxygen via face mask for induction of sedation and 4% for maintenance via nasal cannula and Group KMP (n=37): received intravenous ketamine (1mg/kg), midazolam (0.05mg/kg) and propofol (1mg/kg) combination as induction doses and incremental doses of propofol alone (0.5 mg/kg) IV for maintenance of sedation as needed. The recovery time from sedation and complications were compared. Results: The duration of recovery was significantly shorter in Group S than in group KMP (11.17±1.95 minutes versus17.09±2.50, P<0.001). Regarding complications, there were no significant differences between the two groups, however the incidence of oxygen desaturation was higher in the group KMP (13.5%) than in group S.(5.4 %), but it was statistically non-significant (P, 0.233) Conclusion: Sedation technique using inhalation of sevoflurane provides faster recovery from sedation and more safety than intravenous ketamine, midazolam, and propofol combination and can be utilized as a safe alternative technique for sedation in children undergoing elective UGE.

Keywords: endoscope**,** inhalationl, intravenous, Children.

INTRODUCTION

Pediatric gastrointestinal (GI) endoscopy is a commonly performed procedure needing deep sedation or general anesthesia. Despite being a relatively safe and needing a short duration, it can produce many complications **[1]**.

During pediatric upper GI endoscopy (UGE), intubation is not usually necessary, preventing a potential source of complications and discomfort for the patients, allowing time saving, and helping in increasing the efficiency of the endoscopic unit **[2]**.

Although intubation is not routinely performed for UGE, a number of problems, including airway obstruction, respiratory depression, laryngospasm, and hypoxemia, could still develop. Children are more likely to experience episodes of hypoxemia due to their increased oxygen consumption, and they are also more susceptible to developing hyperactive airways following the onset of upper respiratory tract infections **[3, 4]**.

Several studies have been performed to determine the most effective technique for procedural sedation regarding the quality, easiness of utilization, recovery characters and safety of sedation, however it seems that there is no clear agreement. Despite intravenous sedatives like ketamine, midazolam, and propofol have been used for endoscopic procedures, there have been few studies that compare them with sevoflurane **[2, 5]**.

Sevoflurane is an inhaled anesthetic with special properties for outpatient procedures in pediatrics. It has a low blood–gas partition coefficient, providing

fast induction and emergence, nice odor that makes the patients more responsive to mask induction, low incidence of airway irritation and stimulation of secretion. In addition it has a safe cardiovascular profile, minimal respiratory depression and minimal effect on protective reflexes of the airway in comparison with intravenous (IV) drugs **[6]**.

Sevoflurane has the benefit of being simple to administer to pediatrics with intellectual problems or needle phobia, who are uncooperable with venous catheterization. These distinctive characteristics would make sevoflurane particularly helpful in providing the deep sedation needed for pediatric gastrointestinal endoscopic procedures **[7]**.

Ketamine is very distinct from propofol. It produces "dissociative anesthesia" and provides analgesic action. It also has a sympathomimetic action and preserves spontaneous breathing, that is vital for procedural sedation **[8]**.

Midazolam is a benzodiazepine derivative. Its action begins within one to five minutes and lasts for nearly half to one hour **[9]**. It has a sedative, hypnotic, anxiolytic and anticonvulsant effects and causes anterograde amnesia **[10]**.

Propofol is a sedative -hypnotic agent that is often used in pediatric for induction, maintenance of anesthesia and for sedation. Due to its fast onset and short duration of action, propofol provides rapid awakening. Furthermore, it has antiemetic properties **[11]**.

However, propofol does not provide analgesia and may raise the risk of respiratory and hemodynamic complications at higher doses **[8]**.

The primary outcome of this study was to compare the recovery criteria from sedation by sevoflurane inhalation versus intravenous ketamine, midazolam and propofol combination in pediatrics undergoing elective UGE. The secondary outcome was to compare the two groups with respect to the hemodynamic changes, effectiveness, complications and pediatric gastroenterologist satisfaction.

METHODS

After obtaining Institutional Review Board approval (IRB#9535) and informed written consents from parents or guardians, we enrolled 76 children in this prospective randomized comparative study. The study was registered at http://clinicaltrials.gov/. The registration number is NCT05474937. The study was performed over seven month period from June to December 2022, in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

The procedures were performed in pediatric gastroenterology endoscopy unit of Zagazig University Hospitals. Inclusion criteria were for with parents or 1st degree relatives' acceptance, pediatric patients aged one to four years scheduled for elective UGE for diagnostic or treatment indications, both genders and related to American Society of Anesthesiologists (ASA) physical status I or II. Exclusion criteria were known airway problems or expected difficult airway, active bleeding from esophageal varices, respiratory or cardiac diseases, neurological disorders, recent upper respiratory tract infection, glaucoma, hypertension, increased intra-cranial pressure and allergy to any of the drugs used in the study.

Vital signs, cardiac, chest condition and airway were all checked during the physical examination. Routine laboratory investigations (complete blood count, serum creatinine, liver function test and coagulation profile) were reviewed. All patients were kept fasting prior to sedation in accordance with the American Society of Anesthesiologists' (ASA) standards (2 hours for clear liquids and water, 4 hours for breast milk and 6 hours for non-human milk and light meal) and no sedative premedication was used.

One hour before taking the child to the procedure room, Eutectic Mixture of Local Anesthetics (with 2.5% of Lignocaine with Prilocaine) cream was placed at the determined place for intravenous (IV) access. All children had an IV cannula during sedation and recovery period.

After routine pre-procedure evaluation, standard monitors were connected and maintained in all patients throughout sedation and recovery including pulse oximetry, noninvasive blood pressure using a cuff of proper size and ECG. Baseline measurements of peripheral oxygen saturation, mean arterial pressure, and heart rate were all taken before commencing sedation. Atropine 0.02 mg/kg was given to all patients after a 24- to 22-gauge cannula was placed and secured. Patients were given lactated Ringer's solution and their fluid requirements were calculated using the "4-2-1 rule".

The patients were randomly assigned into two groups (37 patients in each group): group (S): inhalational sevoflurane group and group (KMP): intravenous Ketamine, Midazolam and Propofol group. A computer generated randomization table was used for random allocation and the allocation was concealed using sequentially numbered opaque and sealed envelopes.

Group (S): Sevoflurane was administered to patients at high initial concentration (7%) through an

appropriately sized face mask (attached to Jackson Rees circuit for pediatrics weighting twenty kilograms or less or Pain circuit for pediatrics more than twenty kilograms) and continuing with this dial concentration until the desired level of sedation was reached, which was determined by the achievement of a modified Ramsay sedation score (MRSS) of 7 to 8 (7—Asleep, reflex withdrawal to a painful stimulus only 8—Unresponsive to external stimulus, including pain) and the relaxation of the jaw during the insertion of the endoscope **[12]**. Sedation was maintained using O2 and sevoflurane at a constant 4% dial concentration through nasal cannula.

Group (KMP): Patients were pre-oxygenated with 100% oxygen for 3 min and then received (1mg/kg) I.V ketamine, (0.05mg/kg) I.V Midazolam and (1mg/kg) I.V Propofol for induction of sedation. Once the Modified Ramsay Sedation Score (MRSS) reached from 7 to 8, the jaw relaxed adequitally for endoscopic insertion, and spontaneous breathing was maintained, the induction doses were considered to be adequate. For maintenance of sedation, patients received incremental doses of propofol alone at a rate of (0.5 mg/kg) I.V as required

After endoscope insertion, oxygenation was maintained through a nasal cannula using a rate of 3-4 liters/minute in the two groups. All patients positioned in left lateral position and all procedures performed by the same pediatric gastroenterologist. Duration of procedure was considered as duration in minutes from insertion to removal of endoscopy.

The effectiveness, safety and recovery profile from sedation were assessed and compared between the two groups.

1-The effectiveness of sedation was evaluated regarding the following:

- Induction time defined from the start of an IV agents or inhalation by sevoflurane until the achievement of MRSS 7 to 8.
- Success of induction of sedation was defined when the Modified Ramsay Sedation Score (MRSS) ranged from 7 to 8 enough to make the jaw relaxed for endoscope insertion.
- Success of maintenance of sedation: when the maintenance doses of either the inhalational or intravenous drugs used were enough to maintain sedation and carry out the endoscopic procedure, maintenance then considered successful.

Failure was defined as switching from one group to another, adding another drug or changing dial settings as indicated in methodology or needing an immediate intubation due to sustained desaturation that could not be reversed by non-invasive methods.

2- Safety was evaluated in terms of the occurrence of complications during or after the procedure. Change in MAP and heart rate by twenty percent from basal measurement, oxygen desaturation, laryngospasm, (wheezing, stridor, and apnea), vomiting and emergence agitation were all defined as complications.

- Oxygen desaturation (SpO2 < 92% for more than 30 seconds) was managed by high flow oxygen (6 L/min). When there was no improvement instantly, we asked the pediatrician to remove the endoscope and then repositioning the patient and performing jaw thrust, suction of secretions, insertion of oral airway and Bag- valve -mask ventilation. If there was no improvement intubation was performed.
- Pulmonary aspiration was suspected when we recognized gastric contents in the oropharynx and the patient started coughing violently either during or soon after an endoscopic procedure and was associated with persistent desaturation and we were planned to treat it immediately by intubation, suctioning through ETT and referring to the ICU.
- Bradycardia was defined as a twenty percent decrease in heart rate from its baseline, and it was planned to treat it with intravenous atropine (0.02 mg/mg).
- Hypotension was defined as a 20% decrease in mean arterial pressure from the baseline, and it was planned to treat it with intravenous ephedrine (0.3mg/kg).
- Post procedure vomiting: It was evaluated using a numeric rank score (0 = no vomiting, 1 = vomiting occured once and 2 = vomiting occurd twice or more **[13]**. For vomiting patients were given ondansetron 0.1 mg/kg. Nausea was not recorded because it was difficult to be assessed in children.
- Post procedure emergence agitation were assessed every 5 min post sedation and rated using four point scale (1=Calm, 2= Not calm, but could be easily calmed,3= Moderately agitated or restless, 4=Combative, excited, disoriented) (14). Children having a score of 3 or 4 were considered as agitated.

Recovery profile: the following times were all recorded every two min starting from the end of procedure; a) the emergence time (i.e., time lasting from the end of procedure till reaching MRSS ≤ 3), b) the time to response to light painful stimuli, c) the time to eye opening spontaneously, d) the time to purposeful limb movements, e) recovery time: (time from end of procedure until acheiving Steward Recovery Score 6 (awake, cough on command or cry, purposeful movement) **[15]**.

Post sedation care: patients were monitored in the same room after the procedure was finished until an eye opening or spontaneous verbalization took place. After being returned back to their parents, the patients were stayed in the recovery room and were assessed every five minutes utilizing the modified Aldrete scale **[16]**. Each of the five categories was granted a score of 0–2 (consciousness activity, circulation, respiration and oxygen saturation) with a maximum score of 10. Once modified Aldrete score of ≥ 9 was achieved, patients were discharged.

Pediatric gastroenterologist satisfaction was assessed at the end of the gastric endoscope by determination of the easiness of the endoscopy utilizing 3 point scale (1: easy, 2: adequate, 3: impossible).

Sample size: assuming the mean time to emergence was 3±1.91 vs. 4.82±3.43 in sevoflurane group vs. propofol and ketamine group respectively **[17]**. At 80% power and 95 % CI, the estimated sample size was 74 patients, 37 patients in each group.

STATISTICAL ANALYSIS

Data were analyzed using IBM SPSS (version 20.). Qualitative parameters were presented using number and percent. The Kolmogorov-Smirnov test was utilized to verify the normality of distribution. Quantitative data was presented using range (minimum and maximum), mean and standard deviation. Chi-square test was used for categorical variables, Student t-test was utilized for parametric variables and Mann Whitney test for non-parametric variables, for comparison between the two studied groups. P-value < 0.05 was taken as statistically significant for the obtained results.

RESULTS

In this study 80 pediatric patients were evaluated for eligibility criteria; 6 patients were excluded (4 patients did not have the inclusion criteria, and two parents refused to participate their children in the study). The remaining 74 patients were randomly allocated into 2 equal groups (37 in each group); group Sevoflurane (group S) and group ketamine, midazolam and propofol (group KMP) **(Figure 1)**.

There were no statistically significant differences between the two groups regarding patients characteristics or duration of the procedure (P>.0.05) **(Table 1)**.

There were no statistically significant differences between the two groups regarding patient's indications for the upper gastrointestinal endoscopy (P>.0.05) **(Table 2)**.

Success of induction of sedation was achieved in all patients of the two groups.

Success of maintenance: Group (S) showed that 33 patients (89.2%) had success of maintenance, while 4 had failure of maintenance, one of them due to desaturation and urgency for intubation and in three patients we needed to change to intravenous anesthetics or change in dial settings. In Group (KMP) all patients had success of maintenance except one patient who with desaturation mandating intubation. There were no statistically significant differences between groups (P- value 0.165) **(Table 3)**.

Regarding the heart rate, the basal heart rate was comparable in the two groups (P 0.088), however it was statistically significantly less in Group (KMP) in comparison to Group (S) at the 5^{th}, 10^{th} ,15^{th} , 20^{th}, 25^{th} and 30^{th} minute post-induction (P<0.001*) **(Figure2)**.

Mean arterial blood pressure (MAP), showed no statistically significant differences between the two groups of basal reading and at 5, 10, 15 minutes after induction (P 0.717, 0.296, 0.495 and 0.343 respectively). But, there were statistically significant differences between the two groups at 20, 25 and 30 minutes after induction (P 0.012, 0.002 and <0.001 respectively), as MAP was significantly lower in Group (KMP) compared to Group (S) **(Figure 3)**.

Time of induction was highly statistically significantly lower in Group (KMP) compared to Group (S), (P<0.001). Time for responding to a light painful stimulus, time to reach emergence, time for eye opening spontaneously, time to a purposeful limb movement and recovery time from sedation were highly statistically significantly lower in Group (S) compared to Group (KMP) (P<0.001) **(Table 4)**.

Complications in Group (S) showed that 2 (5.4%) had desaturation, 2 (5.4%) had procedural interruption, 1 (2.7%) had vomiting, 5 (13.5%) had emergence agitation, 2 (5.4%) had laryngospasm, 1 (2.7%) had intubated and 3 (8.1%) were failure while in Group (KMP) 5 (13.5%) had desaturation, 4 (10.8%) had procedural interruption, 3 (8.1%) had vomiting, 1 (2.7%) had emergence agitation, 2 (5.4%) had apnea, 2 (5.4%) had laryngospasm and 1 (2.7%) had intubated. There were no statistically significant differences between groups in complications (P>0.05) **(Table 5)**. Aspiration did not occur in any patients of the two groups.

There were no statistically significant differences between groups regarding pediatric gastroenterologist satisfaction (P>0.05).The endoscopy was easily performed in 33 (89.2%) and 31 (83.8%) in patients in group S and KMP respectively and done adequately in the other

patients. No patients in the two groups were impossible to be performed.

Table (1): Patient characteristics among the two studied groups and duration of the procedure

Variable	Group (S) (n = 37)	Group(KMP) (n = 37)	*Test*	*P* value
Age (years)	2.39±1.11	2.74±1.092	t=1.32	0.188
Gender: Male/Female	20(54.1%)/ 17(45.9 %)	18(48.6%)/19 (51.4%)	χ^2	0.816
ASA I/ II	33(89.2%)/4 (10.8%)	37(100%) / 0(0%)	χ^2	0.115
Weight (kg)	10.17±2.13	10.33±2.28	t= 0.341	0.734
Height (cm)	88.9±8.89	87.8±8.38	t=0.452	0.653
Duration of procedure (minutes)			**U**	
Min.-Max	13.0-20.0	10.5-24.0	677.00	0.847
Mean± S.D	16.62±1.685	16.80±2.778		

Data are presented as mean± SD (standard deviation), number (percentage), or minimum- maximum S= sevoflurane **KMP= Ketamine, Midazolam, Propofol.** T= Independent sample t- test χ^2 :Chi square test, **U:** Mann whitey. There were no statistically significant differences between the two groups (p-value >0.05)

Table (2): Comparison between two groups regarding patient's indications for the upper gastrointestinal endoscopy

Indications	Group (S) (n = 37)		Group (KMP) (n = 37)		P Value	
	No.	**%**	**No.**	**%**		
Diagnostic indications						
Repeated vomiting	18	48.6	12	32.4	0.155	0.053
Abdominal distension	6	16.2	1	2.7	0.047*	
Recurrent abdominal pain	0	0	3	8.1	0.073	
Melena	2	5.4	1	2.7	0.572	
Therapeutic indication s						
Dilatation of esophageal stricture	10	27	17	45.9	0.09	
Esophageal varices	1	2.7	3	8.1	0.304	
Total	37	100	37	100		

Data are expressed as number (percentage) S= sevoflurane, **KMP= Ketamine, Midazolam, Propofol.** The test used: Chi square test. There were no statistically significant differences between the two groups (p-value 0.053)

Table (3): Comparison between two groups as regard to patient's Success of maintenance

Success of maintenance	Group (S) (n = 37)		Group (KMP) (n = 37)		P Value
	No.	%	No.	%	0.165
Succeed	33	89.2	36	97.3	
Failed	4	10.8	1	2.7	

Data are expressed as number (percentage) The test used :Chi square test S= sevoflurane **KMP= Ketamine, Midazolam, Propofol.** There were no statistically significant differences between the two groups (p-value >0.05)

Table (4): Comparison between the two studied groups regarding patient's time of induction and recovery profile

	Group (S) (n = 37)	Group (KMP) (n = 37)	Test of Sig.	P Value
Time of induction (minutes)				
Min.-Max.	2.00-3.30	0.60-0.80	U=0.00	<0.001*
Mean± S.D	2.65±0.37	0.72±0.083		
Time for response to light painful stimuli (minutes)				
Min.-Max.	3.50-7.50	4.50-11.00	t=6.140	<0.001*
Mean± S.D	5.13±1.140	7.28±1.747		
Time of emergence (minutes)				
Min.-Max.	3.90-8.10	5.50-12.30	U=132.00	<0.001*
Mean± S.D	5.71±1.138	8.35±1.837		
Time to spontaneous eye opening (minutes)				
Min.-Max.	4.20-9.00	6.00-17.00	U=112.00	<0.001*
Mean± S.D	6.67±1.290	10.42±2.580		
Time to purposeful limb movement (minutes)				
Min.-Max.	6.00-11.00	8.00-18.00	U=114.00	<0.001*
Mean± S.D	8.52±1.434	12.52±2.723		
Recovery time (minutes)				
Min.-Max.	8.00-14.00	11.40-22.00	t=11.110	<0.001*
Mean± S.D	11.17±1.951	17.09±2.509		

Data are expressed as mean ± SD (standard deviation) or minimum-maximum **U:** Mann- Whitney test , **t:** student t- test, S; sevoflurane, **KMP; Ketamine, Midazolam, Propofol** **P**: p value for comparing between the two studied groups***:** highly statistically significantly different between the two groups P<0.001

Table (5): Comparison between the two groups regarding complications

Complications	Group (S) (n = 37)		Group (KMP) (n = 37)		P Value
	No.	%	No.	%	
Desaturation	2	5.4	5	13.5	0.233
Procedural Interruption	2	5.4	4	10.8	0.394
Vomiting	1	2.7	3	8.1	0.304
Emergence agitation	5	13.5	1	2.7	0.088
Apnea	0	0	2	5.4	0.157
Laryngospasm	2	5.4	2	5.4	1.000
Intubation	1	2.7	1	2.7	1.000
Change to other group	3	8.1	0	0	0.077

Data are presented as number (percentage), S; sevoflurane, **KMP; Ketamine, Midazolam, Propofol.** The test used: Chi square There were no statistically significant differences between the two groups (p-value >0.05).

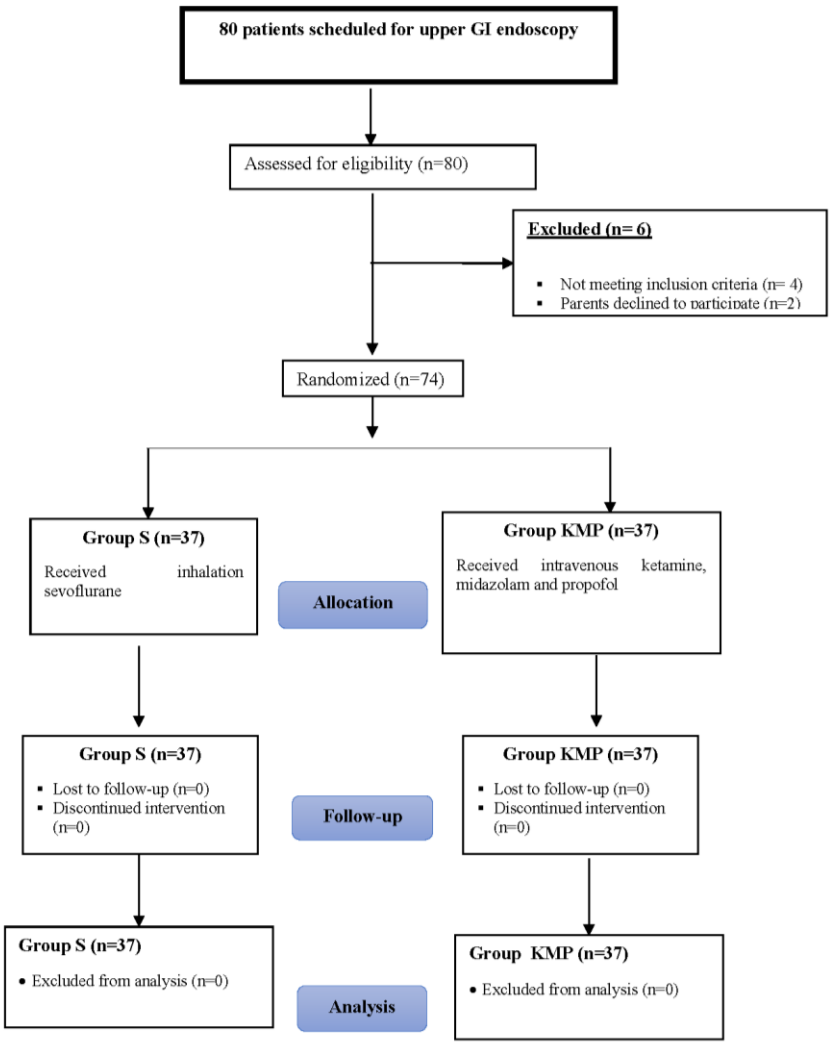

Figure (1): Patients flowchart diagram.

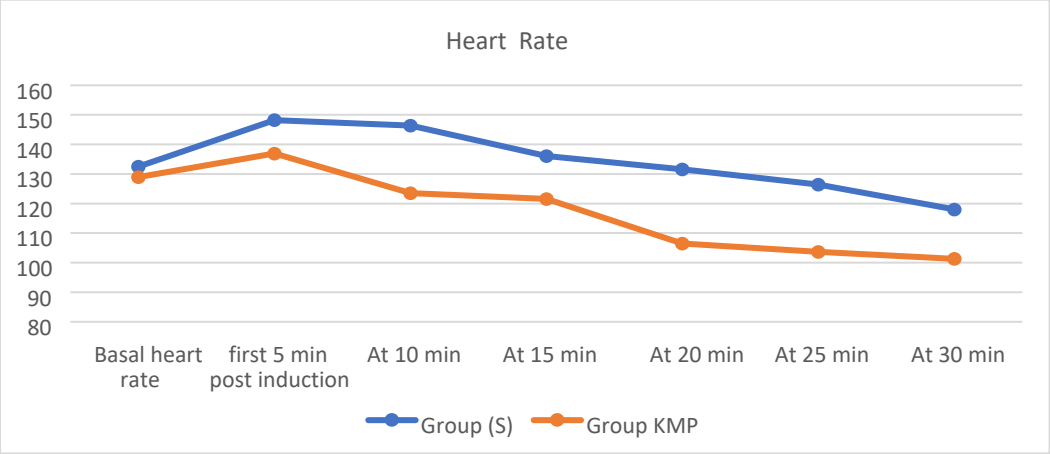

Figure (2): Comparison between the two groups regarding patient's heart rate. S= sevoflurane **KMP= Ketamine, Midazolam, Propofol** Basal heart rate was non- significant in the two groups (P,0.088) but was significantly lesser in Group (KMP) in comparison to Group (S). at 5 ,10 ,15, 20, 25 and 30 minutes after induction (P<0.001*)

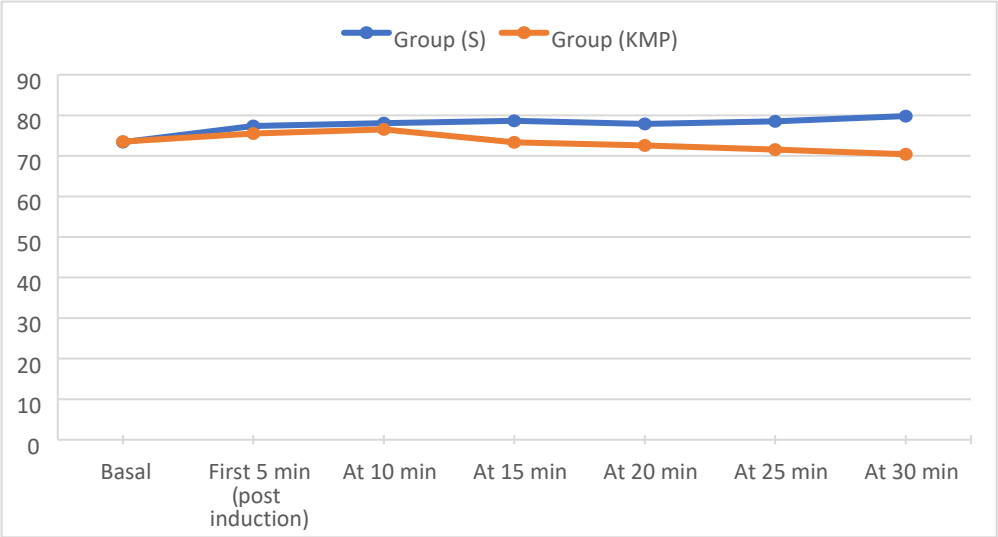

Figure (3): Comparison between the two groups regarding patient's mean arterial blood pressure (MAP). S= sevoflurane KMP= Ketamine, Midazolam, Propofol No significant differences between groups of basal reading and at 5, 10, 15 minutes after induction (P-value. 0.717, 0.296, 0.495 and 0.343 respectively).But MAP was significantly lesser in Group (KMP) in comparison to Group (S).at 20, 25 and 30 minutes after induction (P- value, 0.012, 0.002 and <0.001 respectively.

DISCUSSION

In this study we compared inhalation of sevoflurane with IV ketamine, midazolam and propofol combination for sedation in pediatrics scheduled for elective UGE. Our primary outcome was to compare time to recovery from sedation between the two groups, which may influence the rapidity of turnover and the total number of patients performed per day in pediatrics endoscopy unit.

We found that the duration of recovery was significantly shorter in S Group than in (KMP) group (11.17±1.95 minutes versus17.09±2.50, P<0.001) and there were no significant differences in complications, between the two groups, however the incidence of oxygen desaturation was higher in the group (KMP) (13.5%) than in group (S) (5.4 %) but statistically non-significant (P 0.233). No significant differences detected between the two groups regarding pediatric gastroenterologist satisfaction.

In terms of hemodynamic parameters, the results of this study showed a statistically significant differences between the two studied groups regarding heart rate at 5,10,15,20,25 and 30 min after induction of sedation (P<0.001) as they were significantly lower in Group (KMP) when compared

to Group (S). Mean arterial pressure (MAP), showed no significant differences between the two groups at basal readings and 5,10,15 min after induction of sedation, but there were statistically significant differences between groups at 20, 25 and 30 min post induction (significantly decreased in group KMP). Our results may be explained by the little hemodynamic changes caused by sevoflurane, also the deep level of sedation achieved by adding ketamine and midazolam in addition to propofol may cause parasympathetic activation and myocardial depression and lower blood pressure and heart rate.

Our results were in agreement with the study of Baltaci et al **[18]**, which was conducted on Sixty-one patients scheduled for endoscopic retrograde cholangiopancreatography (ERCP) (group I received IV propofol and group II received sevoflurane inhalation) with sedation regulated by the Ramsay sedation scale (RSS). In their study the systolic blood pressure, although it was less in propofol group in comparison to sevoflurane group at 10th, 20th, 30th & 40th min post sedation, but the difference was statistically non-significant.

In this study the time of induction was highly statistically significantly lower in group (KMP) compared to group (S), (P<0.001). There were highly statistically significant differences between the two groups regarding the time for responding to a painful light stimulus, time to emergence, time to reach eye opening spontaneously, time to purposeful limb movement and recovery time from sedation. All these times were highly statistically significantly lower in group (S), in comparison to group (KMP), where the P value <0.001. Sevoflurane has a lower blood and lipid solubility characteristics, it may help to explain why in the sevoflurane group, recovery was faster.

Our results were in accordance with the results of Chugh and Malde **[17]** .They conducted a study included 60 children aged 6 months to18 years undergoing gastrointestinal endoscopy. They randomly allocated the patients into two groups: Group PK given a combination of ketamine and propofol as initial bolus followed by repeated doses of propofol for maintenance of sedation. Group S were given sevoflurane and nitrous oxide initially and sevoflurane alone for maintenance. Their results showed that all times of recovery including (time for responding to a light painful stimulus, time of emergence, time to reach opening eyes spontaneously, time to limb movement purposefully and recovery time) were significantly shorter with sevoflurane than a combination of ketamine and propofol (P<0.001).

Our results were also in agreement with study of Montes and Bohn **[2]**, as they reviewed two hundred forty eight procedures (fentanyl, midazolam and ketamine combination 67, propofol alone 114, and inhalational sevoflurane 67). They revealed that the time (in minutes) to awakening was significantly lower for sevoflurane (sevoflurane 5.70, midazolam + fentanyl + ketamine 47.15, propofol 36.12, (P<0.01).They conclude that sevoflurane inhalation for sedation in children scheduled to gastrointestinal endoscopy, administered by an anesthesiologist is as safe as traditional endoscopy sedation techniques, has lower cost due to significant saving of time, increases turn over in endoscopy unit and prevent the discomfort during intravenous cannulation in children.

Another study of Sheikhzade et al **[19]** compared total intravenous anesthesia (TIVA) with sevoflurane anesthesia regarding the quality of recovery in pediatrics aged two to ten years who scheduled for outpatient operation. They found statistically significant differences regarding time to spontaneous eye-opening (14±4 and 22 ± 5 minutes) and recovery time (25±4 and 35±5 minutes respectively), between their two groups (P<0.001) which corresponded to our results.

While in Baltaci et al **[18]** study, the author reported that the mean time of awakening in patients who underwent ERCP (calculated from the end of the procedure to the patient eye opening) was significantly lower in group propofol than in group sevoflurane (4.74 ± 3.38 minutes versus 8.67 ± 6.72 minutes respectively, P=0.006). The conflicted results may be explained by the use of three drug combinations (ketamine, midazolam and propofol) in our trial to ensure profound sedation sufficient enough to keep the patient immobile. Baltaci et al **[18]** only used propofol for group I, which explains why awakening time was significantly shorter compared to group sevoflurane.

Our study was supported by Liu et al **[20]**, a study conducted on one to six years old outpatient children scheduled for magnetic resonance imaging (MRI). They had two groups: group (S) received sevoflurane via a face mask and group (K) received intranasal ketamine. They found that group (S) had a significantly less recovery time and significantly less time for resuming basal functional status in comparison to group K (P<0.001).

Our results showed that there were no statistically significant differences between the two groups

regarding complications (desaturation, apnea laryngospasm, need for intubation, procedural interruption). We found the incidence of oxygen desaturation was more in the group (KMP) (5 patients, 13.5%) than in the group (S) (2 patients, 5.4%). In spite of being statistically non-significant, this may provide sevoflurane some advantage considering respiratory safety particularly in children with higher risk of respiratory adverse events.

Chugh and Malde **[17]** showed also that the incidence of oxygen desaturation during the upper GI endoscopy was significantly higher in propofol - ketamine group (20.0%) compared with inhalational sevoflurane group (0%), and it was higher than our study. They explained the occurrence of desaturation by the failure of sedation induction or maintenance in the propofol ketamine group.

Sun and Chen **[21]** performed a study to evaluate the efficacy and safety of inhalational sevoflurane anesthesia for treating ankyloglossia in uncooperative pediatric outpatients aged one to six years. They found the incidence of respiratory depression (SpO2 < 90%) was (2.2%) which was lower than our study (5.4%).

Bryan et al **[22]** performed a study including two hundred pediatrics (18 months to 7 years), underwent brain MRI scans. The patients were randomized to receive either general anaesthesia with sevoflurane; (GAS) through a laryngeal mask airway or general anaesthesia with propofol; (GAP) intravenous bolus and infusion for performance of the scan. The incidence of respiratory complications was higher in GAP than in GAS but statistically non-significant and their results were in line with our findings in that there were no statistically significant differences in respiratory complications between the two groups.

In group (S) one patient (2.7%) had vomiting, five patients (13.5%) had emergence agitation, while in group (KMP) three patients (8.1%) had vomiting, and one patient (2.7%) had emergence agitation. Despite the incidence of vomiting was more in the group (KMP) and the incidence of emergence agitation was higher in the group (S), there were no statistically significant differences between the two studied groups.

Many studies have found that the incidence of emergence agitation following sevoflurane anesthesia was high, which is similar to our results. A study of Kocaturk and Keles **[23]** conducted in 120 children aged ≥3 and ≤6 years who scheduled for complete mouth denture rehabilitation. They randomized the patients to either inhalational sevoflurane anesthesia or total intravenous anesthesia (TIVA) based on propofol. They found that the incidence of agitation was significantly higher following sevoflurane in comparison to TIVA (65.5% vs. 3.4%).

Another study by Karam et al **[24]** was conducted on pediatrics (aged six months to seven years old) who were randomized into two groups: the total intravenous anesthesia (TIVA) group and the sevoflurane group. Their study also showed that agitation was higher in pediatrics who were given sevoflurane inhalational anesthesia than in children who were given TIVA anesthesia. They found postoperative nausea and vomiting were greater in the TIVA group, but were not statistically significantly different; which is consistent with our results.

This study has several limitations. One of the limitations is exclusion of children with ASA physical status more than II and more information on safe sedation in these diseased patients are required. Another limitation is that we did not use bispectral index for monitoring of sedation level which is a more reliable than traditional method for control of sedation level.

CONCLUSION

From the results of the present study, we conclude that sedation technique using sevoflurane inhalation provides faster recovery than intravenous ketamine, midazolam, and propofol and can be employed as an alternative technique for sedation in children scheduled for UGE. On the other hand, it's not devoid of potential complications.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest with respect to the authorship and/or publication of this article.

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